in the DNA minor groove that only occasionally exchanged with the bulk appeared to be a major reason for insufficient convergence. However, convergence could be greatly improved by a combination of standard phase space reduction techniques with flattening of the free energy landscape and configurational exchanges using the Hamiltonian replica exchange method. The approach uses an iteratively adapting biasing potential that corresponds to a previously calculated PMF and smoothens the free energy surface in combination with replica exchanges along the reaction coordinate. In contrast to standard US, the combined method resulted in rapid convergence of calculated free energy changes along the separation distance coordinate and excellent agreement of dissociation and association calculations with experimental results.

2042-Pos Board B772
Adaptive Lambda Square Dynamics Simulation: An Efficient Conformational Sampling Method for Biomolecules
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A novel, efficient sampling method for biomolecules is proposed. The partial Multicanonical Molecular Dynamics (partial McMD, Okumura (2008)) simulation was recently developed as an improved generalized ensemble (GE) methods to focus sampling only on a part of a system (GEPS); he expected that the focused sampling reduced the energy space to be sampled and concomitantly increased the efficiency of the conformational sampling. However, the partial McMD has not been tested well except for an alanine dipeptide system. We found that partial McMD did not work well for poly-lysine decapeptide and gave significantly worse sampling efficiency than a conventional GE. Herein, we elucidate the fundamental reason for this and propose a novel GEPS, adaptive lambda square dynamics (ALSD), which can resolve the problem faced when using partial McMD. We demonstrate that ALSD greatly increases the sampling efficiency of the peptide conformation over a conventional GE by scaling of a partial potential energy: electrostatic, van der Waals, and torsion energies relevant to the peptide. We believe that ALSD is an effective method and is applicable to the conformational sampling of larger and more complicated biomolecule systems. Furthermore, ALSD can be available for conformational sampling of biomolecules with intrinsically disordered regions.

2043-Pos Board B773
QM/MM Simulations of Mg and Zn Solvation
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Mg(II) and Zn(II) ions serve a variety of the biological functions, such as signaling, catalysis, and structure. Despite similar ionic radii (0.72 A for Mg(II) and 0.74 A for Zn(II)), these ions bind to different types of ligands; Mg(II) predominantly binds to phosphates, forming species like Mg-ATP while Zn(II) typically binds to cysteine and histidine side chains. Some of the differences in the biochemistry of Mg(II) and Zn(II) ions are apparent in the solvation energies of these ions in water; despite the similar ionic radii, the hydration free energy of Zn(II) is 30 kcal/mol more favorable than Mg(II). In this work, the hydration properties of Mg(II) and Zn(II) have been explored computationally. The performance in the prediction of the energetics and solvation structure of Mg(II) and Zn(II) are compared. The CHARMM non-polarizable force field incorrectly predicts that Mg(II) has the more favorable solvation free energy. The Drude polarizable model improves the description, but still underestimates the relative solvation energy by 17 kcal/mol. Only a QM/MM simulation using the CHARMM/TURBOMOLE code was able to predict the relative solvation energy and structure of Mg(II) and Zn(II) in good agreement with experiment [1]. ETS-NOCV analysis indicates that this difference is due to increased water-to-ion charge transfer interactions in Zn(II) compare to the Mg(II) due to the higher Lewis acidity of Zn(II).
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Relaxation Mode Analysis for a Peptide
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Biopolymers have flexible structures and several varieties of functions. The functions are derived from not only structures but also the structural fluctuations. Therefore, the properties of structural fluctuations of biopolymers are important for understanding the interrelationship between its movement and functions. Principle component analysis is one of the most popular methods for analyzing the static properties of structural fluctuations. The method treats ''static'' information although it is applied in many simulations of protein systems. Relaxation mode analysis developed to investigate ''dynamic'' properties of polymer, homo-polymer, systems [1,2]. In the case of liner polymers, the relaxation phenomena have been studied systematically in terms of the relaxation modes and rates.In RMA, the time correlation matrices of structural fluctuations for two different times are calculated. Then, by solving a generalized eigenvalue problem for these matrices, the relaxation rates and modes are estimated from the eigenvalues and eigenvectors, respectively. Recently, relaxation mode analysis has been applied to protein, hetero-polymer, systems to investigate dynamic properties of structural fluctuations[3,4]. In this poster, we explain relaxation mode analysis for hetero-polymer systems and show the obtained results.
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2045-Pos Board B775
Space-Time Characteristics of the Protein Thermodynamic Quantities Under the Molecular Crowding Condition of Cytoplasm in Extremophiles: Kirkwood-Buff Approach Combined with Molecular Dynamics Simulation
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Biomolecules in cells occupy about 30% of the volume of cytoplasm. Such molecular crowding conditions arise not only from the presence of the macromolecules but also from high concentrations of cosolvents (low molecular weight compounds).
Especially, extremophiles, i.e., organisms living in the extreme environment of deep sea, hot spring and salt lake contain various osmolytes (such as glycerol, sugars, methylamines, ectoines, and amino acids) in their cells. These protect the conformation and the function of biomolecules from environmental stresses, such as high temperature or high pressure. However, the molecular mechanisms by which osmolytes act at the microscopic level are not fully understood yet.
Here, the molecular crowding conditions of the cytoplasm of extremophiles were mimicked by aqueous solution of ectoine (osmolyte found in halophilic bacteria) or TMAO (found in deep sea fishes). Under such conditions, thermodynamic quantities of the protein (preferential hydration, partial molar volume, and transfer free energy) were calculated by Kirkwood-Buff (KB) theory using the atomic trajectories generated by molecular dynamics (MD) simulations [1-3]. The calculated values showed good correspondence with those obtained by experimental measurements. Furthermore, 3-dimensional distribution and time dependency of those quantities were revealed with our developed space-time deconvolution techniques of the KB integrals. These results provide microscopic characteristics of thermodynamic quantities of proteins under the molecular crowding condition in cytoplasm of extremophiles.
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2046-Pos Board B776
Lifting Constraints in Protein Molecular Dynamics Simulations
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Protein dynamics involve both slow conformational as well as fast bond vibrational degrees of freedom. The slow conformational degrees of freedom can safely and efficiently be described using classical nuclei in molecular dynamics simulations. However, this description breaks down for the faster bond motions as quantum effects begin to dominate. To overcome this shortcoming of the classical propagation, fast protein degrees of freedom are routinely removed and replaced by constraints.
In this study, we lifted the constraints from individual protein atoms and investigated the differences between classical, constraint, semi-classical and quantum nuclear motion. To this end, we chose atoms across the high, mid and low frequency regimes of a protein: a light Hydrogen, a tightly bound Oxygen and a low frequency Carbon atom. Nuclear quantum effects were reintroduced to the time dependent potential generated by the protein and the surrounding solvent. Classical and constraint trajectories were generated using a molecular dynamics integrator. The semi-classical solution was obtained by solving the nuclear Schrödinger Equation using coupled coherent state basis sets of varying sizes and the fully quantum solution was calculated on a numerical grid.
The effects of introducing quantum degrees of freedom in protein molecular dynamics simulations were investigated. Position distributions for the different approaches are presented which illustrate the effect of approximating the quantum distributions by constraints and classical particles.